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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,323	03/16/2001	Daniel Keith Burns	PU3562USW	9629

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EXAMINER

JOHANNSEN, DIANA B

ART UNIT PAPER NUMBER

1634

DATE MAILED: 02/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/787,323	<b>Applicant(s)</b> BURNS ET AL.	
	<b>Examiner</b> Diana B. Johannsen	<b>Art Unit</b> 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 02 December 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 14 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11 and 14 is/are rejected.
- 7) ☒ Claim(s) 9 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |                                                                                                                                           |                                                                                         |
|-------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                                               | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                                      | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>1101</u> . | 6) <input type="checkbox"/> Other: _____                                                |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 2, 2003 in response to the Notice of Non-Responsive Amendment mailed November 19, 2003 has been entered.
2. This action is in response to the request for continued examination filed July 23, 2003 and the Amendment filed November 19, 2003. Claims 1-3, 6-7, 9-11 and 14 have been amended, and claims 1-11 and 14 are now pending and under consideration. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims. **This action is non-final.**
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Information Disclosure Statement***

4. Regarding the IDS of November 9, 2001, it is noted that Applicant filed legible copies of document numbers 3-9 with the RCE of July 23, 2003. Accordingly, the documents have been considered, and an initialed and signed copy of the corresponding 1449 is enclosed herewith.

***Claim Objections***

5. Claim 9 is objected to because of the following informalities: the claim does not end with a period. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

6. Claims 1-11 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 are indefinite because it is unclear as to whether the claims are intended to be drawn to a method "of determining a nucleotide sequence of a nucleic acid," as recited in the preamble of claim 1, or to a method of determining the sequence of first and second short sequencing reaction products, as recited in the final process step. Particularly, the relationship between the first and second products and the "nucleic acid" of the preamble is not clear. Further, the claims do not make clear how the sequencing of the two short products results in the determination of the sequence of the "nucleic acid" of the preamble. Clarification is required.

Claims 6-11 are indefinite because it is unclear as to whether the claims are intended to be drawn to a method "of determining the nucleotide sequence of a portion of a nucleic acid," as recited in the preamble of claim 6, or to a method of determining the sequence of a "first sequencing reaction product," as recited in the final process step. Particularly, the relationship between the "first sequencing reaction product" and the "portion of a nucleic acid" of the preamble is not clear. Further, the claims do not

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make clear how the sequencing of the product results in the determination of the sequence of the "portion of a nucleic acid" of the preamble. Clarification is required.

Claims 6-11 are indefinite over the recitation of the term "a first sequencing reaction product" in step e) of claim 6. This same terminology is employed in step d) of the claim, but because step e) refers to "a" first product (rather than clearly referring back to "the" first product of step d)), it is not clear whether the product of step e) is the same as that of step d) (and, accordingly, it is further unclear as to what product is sequenced in step f)). This rejection could be overcome by amending step e) to refer to "the" product.

Claim 14 is indefinite because it is unclear as to whether the claim is intended to be drawn to a method "of determining the nucleotide sequence of a portion of a nucleic acid," as recited in the preamble, or to a method of determining the sequence of a "sequencing reaction product," as recited in the final process step. Particularly, the relationship between the "sequencing reaction product" and the "portion of a nucleic acid" of the preamble is not clear. The claim does not make clear how the sequencing of the product results in the determination of the sequence of the "portion of a nucleic acid" of the preamble. Clarification is required.

### ***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ansorge et al (Nucleic Acids Research 16(5):2203-2206 [1988]).

It is first noted that the specification at page 2 states that "A short sequencing reaction product can be one of 30 or fewer bases."

Ansorge et al disclose sequencing a 21-base pair long oligonucleotide (see entire reference). The method taught by Ansorge et al comprises steps of loading a short sequencing reaction product onto a polyacrylamide gel (a type of "electrophoresis sequencing device") and determining the sequence of the product (see entire reference, particularly pages 2204-2205). While Ansorge et al do not disclose the loading and sequencing of a second short sequencing reaction product, Ansorge et al teach that "A new set of degraded oligomers can be re-loaded on the sequencing gel after a short time (about 30 minutes) and sequenced" and that "The same gel can be used for the sequence determination of up to 50 different fragments" (page 2204). Ansorge et al further teach that the ability to re-use a single gel to sequence many fragments

“represents a significant time saving compared to the standard methods using radioactive labels, requiring new gel and film exposure for each electrophoresis run” (pages 2205-2206). In view of the teachings of Ansorge et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified Ansorge et al’s method so as to have sequenced multiple oligomers on the same gel at intervals of approximately 30 minutes, as specifically suggested by Ansorge et al. An ordinary artisan would have been motivated to have made such a modification for the advantage of saving time when performing sequence, as taught by Ansorge et al, as well as for the advantage of reducing the quantity of materials needed to perform sequencing, and thereby saving money. It is noted that Ansorge et al’s teaching that gels may be reloaded after “about 30 minutes” (page 2205) constitutes the teaching of a “second loading time” following the first loading time at which the first short product is loaded. Further, Ansorge et al teaches the sequencing of oligomers (page 2205), and it is a property of both the degraded 21-mer and the degraded oligomers taught by Ansorge et al that they would constitute short sequencing reaction products, including products “about 20 bases or shorter,” as required by claim 4. It is further noted that while the specification teaches that a short sequencing reaction product “can be one of 30 or fewer bases,” the specification does not provide a concrete, limiting definition of this terminology.

10. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ansorge et al as applied to claims 1 and 4, above, and further in view of Ruano et al (Nucleic Acids Research 19(24):6877-6882 [1991]).

While Ansorge et al clearly teach that their method may be used for sequencing multiple sequencing reaction products on a single gel, Ansorge et al do not teach a first short sequencing reaction product that is "produced from a region comprising a SNP," as required by the claim. Ruano et al disclose methods of genotyping and haplotyping that comprise sequencing multiple SNP-containing regions within a gene in order to determine the identity of nucleotides at particular polymorphic sites (see entire reference, particularly page 6878 and pages 6880-6881). In view of the teachings of Ruano et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Ansorge et al so as to have sequenced multiple fragments produced from SNP-containing regions of a gene, rather than the particular products taught by Ansorge et al. An ordinary artisan would have been motivated to have made such a modification for the advantage of genotyping and/or haplotyping a gene of interest (such as the beta globin gene), as suggested by Ruano et al.

11. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ansorge et al as applied to claims 1 and 4, above, and further in view of Adams et al (Science 252:1651-1656 [6/1991]).

While Ansorge et al clearly teach that their method may be used for sequencing multiple sequencing reaction products on a single gel, Ansorge et al do not teach a first short sequencing reaction product that is "produced from an EST," as required by the claim. Adams et al disclose that the sequencing of ESTs allows the identification of new genetic markers and the determination of the identities of genes expressed in particular



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tissue types (see entire reference, particularly pages 1651-1652). In view of the teachings of Adams et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Ansorge et al so as to have sequenced multiple fragments produced from ESTs, rather than the particular products taught by Ansorge et al. An ordinary artisan would have been motivated to have made such a modification for the advantage of identifying new genetic markers and determining the identities of populations of genes whose expression characterizes particular tissue types, as suggested by Adams et al.

12. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ansorge et al (U.S. Patent No. 5,124,247 [June, 1992]; hereinafter referred to as "Ansorge-2") in view of Ansorge et al.

Ansorge-2 discloses enzymatic methods of nucleic acid sequencing that comprise steps of loading sequencing reaction products onto a gel (a type of "electrophoresis sequencing device") and determining the sequence of the products (see entire reference, particularly col 1, lines 5-18; col 2, line 49-col 3, line 11; col 4, line 55-col 5, line 9). Ansorge-2 teaches that gels may be re-loaded with a different set of sequencing products after the sequencing of a first set of products, and thereby teaches the loading of gel lanes with different sequencing products at first and second loading times (see col 5, lines 1-9). While Ansorge-2 does not exemplify such re-use of a gel, an ordinary artisan would have been motivated to have modified the method exemplified by Ansorge-2 so as to have re-used a gel in the sequencing of a different set of products because Ansorge-2 specifically suggests doing so. Further, as the enzymatic

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sequencing methods taught by Ansorge-2 produce populations of sequencing reaction products that include products as short as one nucleotide longer than the primer employed in the methods, Ansorge-2 teaches products that are "short" as required by the claim. However, given the length of the target molecule sequenced by Ansorge-2, the practice of Ansorge-2's methods would not be expected to produce a "run off sequencing reaction product," as required by claim 5. Ansorge et al disclose the sequencing of short target molecules such as oligomers (see entire reference, particularly page 2205). It would have been *prima facie* obvious to one of ordinary skill in the art to have modified the method of Ansorge-2 so as to have employed the method in sequencing any type of target molecules, including oligomers, as taught by Ansorge et al, for the advantage of rapidly determining the nucleotide sequences of said molecules. Further, given the small size of the target molecules taught by Ansorge et al, the use of the enzymatic method of Ansorge-2 in sequencing such molecules would produce run off sequencing reaction products. Accordingly, the combined teachings of Ansorge-2 and Ansorge et al suggest the invention of claim 5.

### ***Conclusion***

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read "Diana B. Johannsen", followed by a long horizontal line extending to the right.

Diana B. Johannsen  
Patent Examiner  
February 9, 2004